

2. A particulate composition according to claim 1 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 20°C.

3. A particulate composition according to claim 2 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 40°C.

4. A particulate composition according to claim 1 further comprising a surfactant selected from the group consisting of nonionic detergents, nonionic block copolymers, ionic surfactants and combinations thereof.

5. A particulate composition according to claim 4 wherein the surfactant is selected from the group consisting of sorbitan esters, ethoxylated sorbitan esters, fatty acids, salts, sugar esters, ethylene oxides, and combinations thereof.

8. A particulate composition according to claim 1 wherein the polyvalent cation is a divalent cation.

9. A particulate composition according to claim 8 wherein the divalent cation is selected from the group consisting of calcium, magnesium, or zinc.

10. (Amended) A particulate composition according to claim 8 wherein the molar ratio of divalent cation to phospholipid is at least 0.05.

11. (Amended) A particulate composition according to claim 10 wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.

12. (Amended) A particulate composition according to claim 10 wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.

13. A particulate composition according to claim 12 wherein the divalent cation is calcium.

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*A3 Sub B cont*

14. (Amended) A particulate composition according to claim 13 wherein the molar ratio of calcium to phospholipid is about 0.50.

15. A particulate composition according to claim 1 wherein the phospholipid comprises a natural or synthetic lung surfactant.

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16. (Amended) A particulate composition according to claim 1 further comprising an active agent.

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17. (Amended) A particulate composition according to claim 16 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

18. A particulate composition according to claim 1 further comprising a polymer selected from the group consisting of polysaccharides, polyvinyl alcohol, polyvinyl pyrrolidone, polylactides, polyglycolides, polyethylene glycol, or mixtures thereof.

19. A particulate composition according to claim 1 comprising particles having a mass median diameter of less than 20 microns.

20. A particulate composition according to claim 19 wherein the mass median diameter is within 0.5 – 5 microns.

21. A particulate composition according to claim 19 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

22. A particulate composition according to claim 21 wherein the aerodynamic diameter is within 0.5 – 5 microns.

23. A particulate composition according to claim 1 comprising an emitted dose of at least 40%.

24. A particulate composition according to claim 1 comprising an emitted dose of at least 60%.

25. A particulate composition according to claim 1 comprising an emitted dose of at least 90%.

26. A particulate composition according to claim 1 further comprising a non-aqueous suspension medium.

27. A particulate composition according to claim 1 further comprising an excipient selected from the group consisting of amino acids, carbohydrates, inorganic salts, organic salts, carboxylic acids, and mixtures thereof.

28. A particulate composition according to claim 27 wherein the excipient is selected from the group consisting of hydrophobic amino acids, monosaccharides, disaccharides, polysaccharides, sodium citrate, citric acid, ammonium carbonate, ammonium acetate, and ammonium chloride.

29. A particulate composition according to claim 1 further comprising a density of less than 0.5 g/cm<sup>3</sup>.

30. A particulate composition according to claim 29 wherein the density is less than 0.05 g/cm<sup>3</sup>

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31. (Amended) A particulate composition comprising:  
biodegradable particles comprising a phospholipid and a polyvalent cation wherein the composition comprises a gel-to-liquid transition temperature T<sub>m</sub> and a storage temperature T<sub>s</sub> wherein T<sub>m</sub> > T<sub>s</sub> by at least 20 °C.

32. (Amended) A particulate composition for delivery to the pulmonary system comprising:  
20 – 99.9% of a saturated phospholipid;  
a polyvalent cation in an amount effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation; and, optionally 0.1 – 80% active agent;

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A7*  
wherein the composition is in the form of hollow and porous particles.

44. (Amended) A method for delivery to the pulmonary system comprising administering to the respiratory tract of a patient in need of treatment an effective amount of storage stable particles comprising a saturated phospholipid and a polyvalent cation present in an amount effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation.

45. A method according to claim 44 wherein the particulate composition comprises particles having a mass median diameter of less than 20 microns.

46. A method according to claim 45 wherein the mass median diameter is within 0.5 – 5 microns.

47. A method according to claim 45 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

48. A method according to claim 47 wherein the aerodynamic diameter is within 0.5 – 5 microns.

49. A method according to claim 44 wherein the particles comprise polyvalent cation at a molar ratio of cation:phospholipid of 0.25-1.0

50. A method according to claim 49 wherein the polyvalent cation comprises calcium.

51. A method according to claim 48 wherein the particles comprise a density of less than 0.5 g/cm<sup>3</sup>.

52. A method according to claim 51 wherein the particles further comprise an active agent selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol and salts thereof.

53. (New) A particulate composition according to claim 1 wherein the particles are hollow and porous.

54. (New) A particulate composition according to claim 16 comprising 0.1 – 80% w/w of an active agent.

55. (New) A particulate composition according to claim 31 wherein the particles are hollow and porous.

56. (New) A particulate composition according to claim 31 wherein the storage temperature is approximately room temperature.

57. (New) A particulate composition according to claim 56 wherein  $T_m > T_s$  by at least 40 °C.

58. (New) A particulate composition according to claim 56 wherein the phospholipid is selected from dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

59. (New) A particulate composition comprising a structural matrix comprising a saturated phospholipid and a polyvalent cation in an amount effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation, wherein the composition is storage stable.

60. (New) A particulate composition according to claim 59 wherein the phospholipid comprises dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

61. (New) A particulate composition according to claim 59 wherein the polyvalent cation is a divalent cation.

62. (New) A particulate composition according to claim 61 wherein the divalent cation is selected from the group consisting of calcium, magnesium, or zinc.

63. (New) A particulate composition according to claim 62 wherein the molar ratio of divalent cation to phospholipid is at least 0.05.

*Sub 1  
contd*

*AS  
O/P/M*

64. (New) A particulate composition according to claim 63 wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.
65. (New) A particulate composition according to claim 63 wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.
66. (New) A particulate composition according to claim 59 further comprising an active agent.
67. (New) A particulate composition according to claim 66 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.
68. (New) A particulate composition according to claim 61 wherein the divalent cation is calcium.
69. (New) A particulate composition according to claim 68 wherein the molar ratio of calcium to phospholipid is about 0.50.
70. (New) A particulate composition according to claim 59 wherein the composition comprises a gel-to-liquid transition temperature  $T_m$  and a storage temperature  $T_s$  wherein  $T_m > T_s$  by at least 20 °C.
71. (New) A particulate composition according to claim 70 wherein  $T_m > T_s$  by at least 40 °C.